American Journal of Pharmacy

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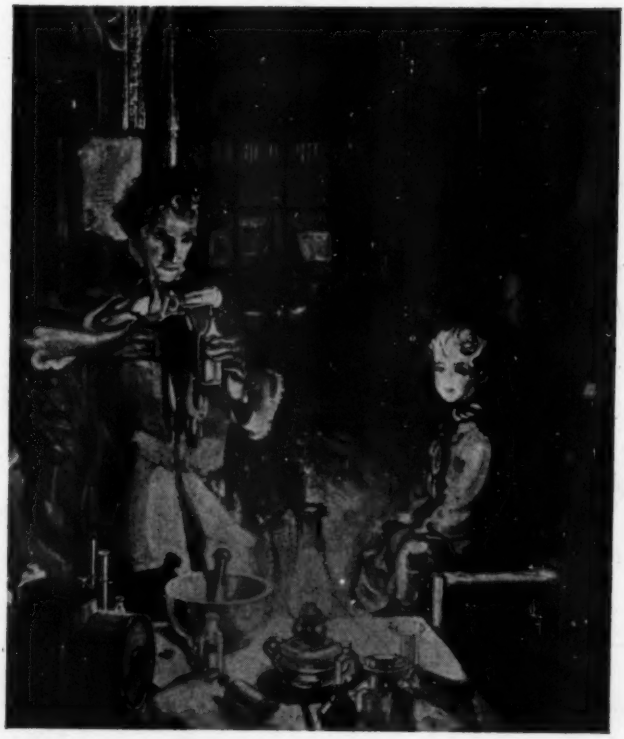

Since 1825

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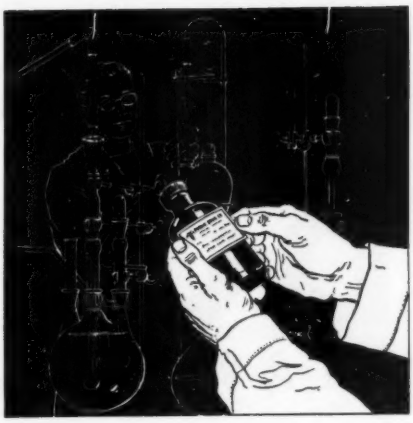

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AND THE SCIENCES SUPPORTING PUBLIC HEALTH

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CONTENTS

E D I T O R I A L

THE F. D. A. RULING ON REFILLS.

FROM time to time we have taken keen exception to certain interpretations of the Food, Drug and Cosmetic Act by those officials responsible for its implementation and enforcement. Thus we were among the first, if not the first, to attack the ruling requiring a warning statement on the label of a prescription for a thiouracil. In this connection, it is interesting to note that medical and pharmaceutical opinion, at first seemingly apathetic, has finally crystallized sufficiently so that corrective legal action is being considered.

The Food and Drug Administration, bolstered by the favorable Supreme Court decision on the now famous Sullivan Case, has been looking more and more closely into the conduct of pharmacy on the retail level, judging that it, the F. D. A., has the authority to regulate all practices from producer to the ultimate consumer. It is not surprising that some of the practices in the filling of prescriptions were found wanting.

A recent ruling by Commissioner Dunbar in effect states that prescriptions that are refilled without the express authority of the prescribing physician are to be dispensed by the pharmacist only upon the condition that he, the pharmacist, assumes full responsibility for the act. This means that on many drugs the regular prescription label used the first time the prescription was filled will not be adequate. A new label must be prepared giving adequate directions for use and all warning statements needed. What is even more serious, any damage resulting to the patient will be the responsibility of the pharmacist and not the physician.

Although we risk the ire of the whole pharmaceutical profession, we must agree with Commissioner Dunbar in this case. The prescription refill evil has been a disgrace to our profession for years. We ourselves have not corrected it because of the short-sighted belief that to do so would cut prescription volume. The truth is that many physicians refuse to write prescriptions or do so only rarely because they know that once a patient is so armed with an order for

medication the physician often loses control of the case. Only too often he finds his former patient, months later, still taking the same medication and even prescribing it for his friends whose ailment he, the patient, has diagnosed as identical with his own. Some physicians are known to deliberately add codeine sulfate to a prescription to put it in the narcotic category so that it cannot be refilled. For every pharmacist that honors the *non repetatur* subscript some other one less scrupulous will ignore it.

Commissioner Dunbar is correct in spiking this evil. It protects the public from the dangers of self-medication with the most hazardous of all medications for lay use, prescription drugs. Physicians, in all likelihood, will endorse the ruling for it protects both their patients as well as themselves from an acknowledged danger. If pharmacists will examine this ruling with reason instead of self-interest it will be seen that no pharmacist has ever had the moral or ethical right to refill a prescription unless it was the express will of the prescriber. This ruling in no way alters what should always have been our approach to the correct physician-pharmacist-patient relationship.

When it can be definitely and permanently established that no prescription will be refilled without absolute certification by the prescriber, we predict that there will be a significant and continuing increase in prescription writing. Those who are now contemplating vigorous action to upset this ruling on refills would do well to study this matter more objectively before taking action that may appear not motivated by professional or public interest. Although we may question the means used by the F. D. A. to correct the refill evil, we must recognize that it is indeed an evil and that it demands correction.

L. F. Tice

CURRENT TRENDS IN MODERN MEDICINALS

By Madeline O. Holland, D. Sc.

(Part II*)

ANTICOAGULANTS—COAGULANTS

Heparin

Heparin is an old drug but one for which new uses have been found. The intravenous or subcutaneous (into the lesion) injection of heparin was found to prevent gangrene in patients with experimental frostbite lesions. Heparinization after the lesions had been warmed to room temperature for 24 hours gave almost as good results as with immediate heparinization. The general technic of administration comprised the injection of 20-25 drops per minute of a solution containing 300 mg. of heparin in 2,000 cc. of physiological salt solution. All of the solution was given over a period of 24 hours. Clotting time was maintained between 30 and 60 minutes.

Algarin

The sodium salt of an alginic acid disulfuric ester which contains 15 to 17 per cent of sulfur has been found to have a powerful anticoagulant action *in vivo* as well as *in vitro*. Known as Algarin, this drug differs from heretofore described substances of this class because of its relatively low toxicity and failure to produce hemorrhage of the viscera. When injected intravenously in large doses the blood pressure is not affected. Algarin is not inactivated by the liver and is 1/5 to 1/12 as active as heparin dependent upon the species employed. Practically identical intensity and duration of effect are attained for both drugs when these ratios are employed. Injections of protamine sulfate or toluidine blue act as antidotes. Algarin is being investigated by the Wyeth Institute of Applied Biochemistry.

Rutin

In previous articles rutin has been discussed at length. However, mention must be made of the new use which has developed for this product. Studies of the irradiation-induced hemorrhage fol-

* Part I of this annual review was published in the November issue.

lowing exposure to ionizing radiations, as described under another subject, have shown that control of vascular integrity might be of benefit in this state of hypocoagulability. Prevention of vascular damage might reduce hemorrhagic extravasation since the function of certain critical organs already was impaired by direct destruction from the ionizing irradiation and further injured by bloody ooze of capillary destruction. The opportunity for eventual restoration of organ function would be extended if the vascular structure was maintained. Rutin was found to bring about recovery in such experiments on dogs. It is therefore believed that it will prove of value as a prophylactic for x-ray, radium and atomic research workers since overexposure to radiations of radium or other materials emitting short-wave energy like x-rays frequently leads to hemorrhage due to weakening of the capillaries. Rutin is available in various forms and combinations from numerous firms.

Toluidine Blue

Exposure of the entire body to ionizing radiations in the midlethal range results in a syndrome of which one of the most striking features is hemorrhage. This phenomenon occurs in both man and experimental animals. A thrombocytopenia accompanies the hemorrhage as well. Bleeding and clotting times are prolonged and clot retraction is impaired. This effect appears to be due to the development of an anticoagulant in the blood which is biologically indistinguishable from heparin rather than caused by the thrombocytopenia as previously thought. Extensive exposure may even render the blood entirely incoagulable. Extensive investigation of this condition has resulted in the use of substances such as toluidine blue, other members of the thionine series and protamine which possess clotting properties in restoring the clotting time to normal both *in vivo* and *in vitro*. Further studies revealed that the administration of vitamin K, ascorbic acid, calcium salts and fresh whole blood transfusions did not prevent the onset of hemorrhage or stop the bleeding once it had started. In a test animal it was found that a clotting time of more than 48 hours could be restored to normal within 20 minutes after 24 mg. of toluidine blue had been given. These observations led to further work on the possible effect of this dye on hemorrhagic manifestations associated with such diseases as thrombocytopenia and acute leukemias. The results first obtained in early studies have

shown that it is possible to induce temporary alleviations of the hemorrhagic manifestations.

The nitrogen mustard drugs, when given in cases of neoplastic disease, have also been found to cause an anticoagulant effect similar to that produced by radiation. In such cases it was found that toluidine blue, given intravenously in a dose of 2 mg. per Kg., was sufficient to restore the clotting time to normal for a 24-hour period. In order to maintain the normal clotting time a maintenance dose of 2 mg. per Kg. or more was given every 24 hours.

ANALGESIC—ANESTHETICS

Surfacaine

The field of anesthesia is a very broad one and new agents for producing it are introduced periodically. One such drug made available in the past year is a local anesthetic agent which acts on damaged or diseased skin and on rectal mucous membrane. It provides effective topical anesthesia for abrasions, burns, and certain types of superficial skin lesions and for all painful rectal conditions in which the pain arises in the mucous membrane or ulcerated fissures. Cyclomethycaine belongs chemically to the group of substituted piperidinoalkyl benzoates. This drug is available in ointment, jelly, cream and suppository form under the name of Surfacaine from Eli Lilly and Co., Inc.

SKF 538-A

Chemists of Smith, Kline and French Laboratories recently described a new pain-killing drug known chemically as 1-(β-dimethylaminoethoxy)-4-butyl-isoquinoline and possessing a potency many times that of cocaine. Although this drug is still in the experimental stage it does show great possibilities because in dilution as low as one-hundredth of one per cent it produced local anesthesia in rabbits lasting over three hours. This compares with 69 minutes for another anesthetic, dibucaine, 18 minutes for cocaine, and two minutes for procaine.

Arthralgen

The rheumatic and allied disorders are very painful and disabling and difficult to treat. A new product recently introduced contains 0.25 per cent methacholine chloride, 1 per cent thymol, 10 per

cent menthol and 15 per cent methyl salicylate in an absorbable, washable base and is indicated in the local treatment of chronic arthritis, myalgias, arthralgias and neuralgias of sprains, lumbago, muscular injuries, synovitis, bursitis and neuritis. The drug is applied in a thin film twice a day to the affected parts previously warmed by a hot bath or hot wet packs leaving the skin wet. It is claimed that it relieves pain and induces increased blood-flow to affected parts in rheumatic and allied disorders by producing dilatation of both arterioles and capillaries, effecting analgesia and erythema lasting several hours. This product is marketed as Arthralgen by Whittier Laboratories, division of Nutrition Research Laboratories, Inc.

NEW TECHNICS

Hypospray

Recently announcement was made of the development of a mechanical device designed to administer needleless injections under the skin. This apparatus is known as the Hypospray and is at present under carefully controlled clinical investigation. The "Hypospray" is designed to save time and to provide a painless means of injection. It may in the future, after clinically proven, replace the present syringe, needle and puncture method for administering certain parenteral solutions. It resembles in appearance a small tubular flashlight and accomplishes its work by forcing a fine jet of almost microscopic size under high pressure through the dermis into the tissues. The actuating mechanism is a powerful spring which may be adjusted to different tensions in order to obtain various depths of penetration of the medicament. The medication is forced through the skin into the subcutaneous fat with a minimum of tissue damage. The drug and solution are contained in a "Metapule," which is a sterile metal ampule. The latter has an orifice of approximately 80 microns in diameter, or about the size of a fine human hair. The area punctured by a 24-gauge needle is approximately 50 times greater. Thus the Hypospray reduces trauma to an almost imperceptible size and administration may be accomplished with pain rarely experienced by the patient.

The sterile Metapule first has its container cap removed by means of the opener on the barrel of the apparatus. The container

is then inverted over the end of the Hypospray and the Metapule is dropped into clamp jaws without being touched. It is then locked firmly into place in the clamp jaws which cannot be locked unless the Metapule is in proper position. There is a slight excess of medication in the Metapule which will exude from the orifice as the retractor sleeve is turned. A dosage graduation must be followed and if less than the full dose is needed the excess should be expelled by continuing to turn the retractor sleeve counterclockwise.

The injection site should be wiped with alcohol or other suitable antiseptic prior to the preparation of the instrument in order that the site of injection will be dry. Manual stretching of the skin and firm pressure of the rounded Metapule against the site so that the clamp sleeve is almost touching the skin is necessary for skin tension. The Hypospray should be held normal to the surface to be injected. When the instrument is in place, the release button is pressed and held against the site of injection for at least 3 seconds.

When the clamp jaws are turned to "Open," the Metapules are ejected automatically. The apparatus should be cleaned by wiping with alcohol or ether. It is not necessary to sterilize because no moving parts come into contact with the sterile medication. The first piece of apparatus developed administers only 0.5 cc. of medication but a newer device now being completed will administer 1 cc. of medication. The patents on the Hypospray are owned by Becton, Dickinson and Co. with special rights granted to Gelatin Products Division, R. P. Scherer Corp., who are developing it.

Jetomizer

Along with new developments in drugs there are also introduced frequently new pieces of apparatus for their administration. Nasal medication has been a problem because of the difficulty in administering it. The nose dropper is inefficient because the patient can never be sure that the medication will be diffused sufficiently to produce the desired results. Nasal sprays are not always satisfactory either. There has been developed recently a plastic instrument known as a Jetomizer which overcomes many of the difficulties encountered. With this instrument it is possible to deliver a measured jet of 2 to 3 drops of medication with assurance of wide diffusion. The medication is distributed throughout the nasal cavities with no risk of injuring delicate tissue. A transparent sanitary cover protects the

exposed portion so that the instrument can be carried in the pocket or handbag. Each pump stroke delivers approximately 0.16 cc. so that dosage can be fairly accurately controlled. Jetomizer is marketed by Wyeth Inc. and can be used with any clear nasal solution.

Silicosis Treatment

Silicosis is considered to be one of the great killers in the anthracite mines as well as in industries such as iron, lead, zinc and granite mining. Research, conducted over a period of years, has resulted in the development of a device to cure this dread malady. Some 500 hard coal miners permanently disabled by silicosis have been treated with considerable success with the mechanism developed at Jefferson Hospital, Philadelphia. The apparatus is an elaboration of the ordinary nebulizer combined with a pump which aids the patient to breathe. The pump is really an intermittent positive pressure cycling valve originally developed for treating Air Force fliers suffering from lack of oxygen. The valve "breathes" for the patient, pumping oxygen into his lungs and gently sucking out the waste carbon dioxide. Hooked up with the nebulizer, the valve introduces drugs into respiratory tracts which would not otherwise be reached. The ordinary nebulizer is of no value in many cases of silicosis because the lung tissues which are irritated by the silica dust develop congestion and hardening and medicinals cannot be inhaled into the area needed.

Radar Waves

Diathermy has been available for many years and is used in the therapy of bursitis, muscular spasm and localized myositis. Drs. K. G. Wakim, Julia F. Herrick, G. M. Martin and F. H. Krusen recently reported gratifying results in the therapy of these conditions with continuously generated microwaves (12 cm.) at a frequency of 2,450 megacycles per second. The local heating of tissues was associated with increase of circulation in the heated extremity. Microwaves were contraindicated if there is localized fluid in the area to be treated. The Raytheon Microtherm generates energy in a continuous wave, air-cooled magnetron oscillator tube which is the first generator giving this type of wave for the heating of human tissues. The magnetron oscillator tube is the instrument which made radar possible.

Nylon Bandage

Drs. J. P. Bull, J. R. Squire and Elizabeth Topley of the Birmingham, England, Accident Hospital have reported the use of a nylon dressing which is transparent and allows for passage of the water vapor but still is an effective barrier against micro-organisms. The dressings now available are synthetic rubber-like materials which keep the skin surface sodden therefore slowing the healing process. A nylon derivative used by these English workers has shown great promise in this respect. Because it is transparent the wound can be inspected without disturbing the dressing. Dry heat sterilization can be used. Boiling water tends to soften the dressing. Comparative tests with a polythene film showed that in 2 hours water had accumulated under the polythene film whereas the skin under the nylon bandage was normal. The film does not inactivate penicillin *in vitro*. By maintaining a complete seal with this type of bandage the entrance of other infectious organisms is prevented. However sepsis may occur if the wound is already infected before the dressing is applied.

BLOOD PRODUCTS

Kollidon

A blood substitute developed by Weese, head of the pharmacology department of I. G. Farbenindustrie was described as a colloid, polyvinyl pyrrolidone or Kollidon. It is used as a 2.5 per cent colloidal solution under the name Periston. The colloid has a molecular weight of 6,000 to 8,000. It is claimed that Periston saved the lives of thousands of German soldiers as a blood substitute. It may be given to any person irrespective of blood group. It is stable on storage at ordinary temperatures and even under tropical conditions. It is inexpensive, neutral in reaction, and has a high viscosity. The compound is broken down and eliminated by the human body. It is claimed to be absolutely non-toxic.

Ac Globulin

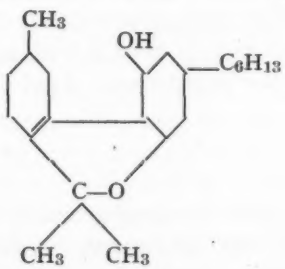
A fifth factor necessary to blood clotting has been discovered. It has been called the fifth coagulation factor or ac-globulin. The ac signifies accelerator since this factor is one of those which sets the clotting process in motion. This new factor has been found of value in treating the rare disease, parahemophilia. In certain heart

conditions the blood has a tendency to clot in the veins which condition is relieved by administration of dicumarol. The ac-globulin is of some value in a two-stage method of more safely treating such patients with dicumarol.

DRUGS USED FOR EFFECTS ON HIGHER NERVE CENTERS

Synhexyl

One of the most common psychiatric conditions encountered is neurotic depression or the syndrome of thalamic dysfunction. It is frequently intractable and difficult to treat effectively. Various euphorigenic drugs have been employed in the therapy of this state because it is believed that a powerful euphorigenic drug would be capable of reversing the thalamic disturbance. However, such a drug should also be free of the objectionable properties found in narcotic compounds. The ideal euphoriant must possess certain specified properties but to date the drugs used have not fulfilled the specifications. The development of new synthetic cannabis-like derivatives of the dibenzopyran class has resulted in a new agent of great promise in psychiatry. The most active pharmacologically of the new compounds is 1-hydroxy-3-*n*-hexyl-6-6-9-trimethyl-7-8-9-10-tetrahydro-6-dibenzopyran with the following structural formula:



The product is a pale-yellow, translucent, very viscous, odorless resin, soluble in organic solvents but insoluble in water, alkalis and acids. The laevorotatory form is several times as active as the dextrorotatory form. The drug is known under the names of Synhexyl, Pyrahexyl or Parahexyl. Synhexyl is more potent weight for weight than natural cannabis, the effective dosage being from 5 to 15 mg. in normal subjects to 60 to 90 mg. in depressive patients.

In narcotic drug addicts doses of 60 to 240 mg. may be given 3 times a day without ill effects. It is most effective by the oral route. When given to depressive patients Synhexyl was found to ameliorate the dysphoria to a greater degree than the other symptoms of obsessional thoughts, pains, paraesthesias, and the like. Although they were little affected they were made less distressing to the patient. Extensive study showed that Synhexyl has a low toxicity, minimum of side effects, ease of administration and chemical stability. Coexisting organic disease does not contraindicate its use and it can be used for out-patient practice. It does not have the risks and disadvantages of the more drastic means of therapy and it may possibly replace such methods for the milder depressions of later life. The disadvantages of Synhexyl include its insolubility, slow and uncertain nature and comparatively weak analgesic effect so that in the more severe forms of sensory thalamic dysfunction it is comparatively ineffective. Synhexyl is under investigation in England by Roche Products, Ltd.

Phenuron

At the recent national medicinal chemistry symposium conducted by the American Chemical Society a new anticonvulsant was announced. Numerous compounds in the various groups of ureides, allophanates and carbamates have been investigated by Abbott Laboratories but phenacetylurea has shown the most promise. This is a synthetic compound made from phenobarbital. Known as Phenuron or Thenuron this drug is now in clinical trial and thus far has been demonstrated to be effective in petit mal, grand mal and psychomotor epileptic seizures.

Glutamic Acid

Although glutamic acid has been available for several years it has aroused considerable interest recently because of its use in the therapy of mental retardation, particularly in children. Rather good results have been attained with its administration in dosages of 12 to 24 Gm. daily. The natural dextrorotatory or *l* + glutamic acid is an amino acid occurring in the form of a white crystalline powder with a mildly acid taste. It is available in 0.5 Gm. tablets from Parke, Davis and Co., Inc.

In experimental studies it was found that when glutamic acid was given each day for 6 months to 69 children and adolescents

ranging in age from 16 months to 17 years, five months (44 mentally retarded and 11 epileptics) their mental development was as much as it would have been without the drug in 13 months. When given to epileptic patients in an attempt to control the convulsions it was found that the patients were more physically and mentally alert. The patients also frequently showed better emotional adjustment.

DRUGS USED IN THE TREATMENT OF CANCER

Diopterin, Gamopterin and Teropterin

A study of the pteroyl glutamic acid compounds conducted over a period of years led to the synthesis of folic acid, a substance which had been isolated from natural sources a short time before. However, this development did not affect adversely the course of research with these compounds for it was believed that other preparations related to folic acid might also have therapeutic value. Consequently, there have been developed by Lederle Laboratories three compounds which have shown some possible value: pteroyl diglutamic acid (Diopterin), pteroyl triglutamic acid (Teropterin) and pteroyl gamma glutamic acid (Gamopterin). As a result of studies conducted on patients suffering with various types of malignancies the triglutamic acid derivative has been made available for investigational use in the palliation of malignancy.

General effects of the compounds particularly on the adult patients, included improvement in energy, appetite, sense of well-being, less irritability and apprehension. Some improvement was attributed to psychotherapy because the patient was impressed with the fact that something more than usual was being done. A definite diminution of pain was noted in a few cases as evidenced by the reduction in the amount of sedation or analgesia necessary.

In a few cases the changes in the patient's condition or in histological appearance of the tumor obtained at biopsy or at autopsy could be attributed to administration of the glutamic compound. In a larger group of patients where other therapeutic procedures were also being used the addition of the glutamic compound was found to play an important role in their improvement. Such changes were not constant but were frequent enough to warrant further investigation.

Use of Teropterin should not preclude the use of all recognized forms of treatment for arresting malignant growth such as radium,

X-ray or surgery but should be employed simultaneously. It is not considered to be a substitute. The recommended dosage plan is 10 mg. (1 cc.) once daily for the first week. Beginning with the second week two 10 mg. injections may be given daily for 3 to 4 weeks when it may be desirable to stop the therapy in order to evaluate the condition and to decide whether or not it should be continued.

For intravenous or intramuscular administration in the clinical trials the substance was dissolved easily in 1 to 8 cc. of saline. When larger doses were given intravenously it was necessary to use as much as 20 cc. of normal saline. The product available now contains 10 mg. in 1 cc. of solution.

A recent statement by the Council on Pharmacy and Chemistry of the American Medical Association reviewed the situation with these drugs because the hope of many sufferers from cancer had been raised that a cure had been found. This body feels that it is too early to conclude that these compounds are effective or ineffective in cancer because there have been an insufficint number of cases observed and the period of study has been too short.

Gamopterin is being tested in the therapy of anemias and metabolic diseases.

Spleen Extract

The spleen is rarely attacked when cancer spreads from other organs therefore it seems logical to suppose that there is something in this organ which resists cancer. For this reason Dr. G. F. Watson of Kitchener, Ont., began to prepare spleen extracts for therapy some eighteen years ago. The first extract showed some promise but another one recently tested has shown more effectiveness. One patient with cancer of the kidney and two with cancer of the lungs were treated with this new extract and showed definite improvement in general health. When tested on transplanted cancer cells in mice the extract was found to cause degeneration of the cells in 48 hours. However, authorities on cancer believe that a more complete and reliable test of efficiency of drugs in cancer is their effect on chemically induced cancer. When tested in this manner the spleen extract affected cell destruction after 3 injections daily for 5 days or 15 injections. No claims have been made that spleen extract is a cure for cancer but some hope is presented in the fact that 2 patients have been kept alive for 12 and 13 years respectively with this therapy.

Urethane

Urethane or ethyl carbamate is the ethyl ester of carbamic acid. This compound, also well known and employed in therapy for years, has found new applications. The drug is freely soluble in water possessing no disagreeable odor, taste or local effects. It has been shown by recent research studies that ingestion of urethane reduced the number of leukocytes in chronic myelogenous leukemia and reduced the size of the spleen and lymph nodes. There is no evidence that the effects are permanent. Abbott Laboratories are offering Urethane U. S. P. Solution for investigational use in the treatment of chronic myelogenous leukemia. It is not recommended for use in acute leukemia or lymphatic leukemia. Treatment may be started with a dose of 0.5 Gm. twice daily in patients with moderately elevated white blood cell counts. If no effect appears in a few days, it may be raised to 0.5 Gm. three times daily. Should no response be noted after 8 to 10 weeks, the drug should be discontinued. In all cases, the leukocyte and red cell counts should be checked frequently. When the leukocyte count has been lowered to 10,000 or 20,000, the dose of urethane should be reduced to the amount that will maintain it at or near normal. In most instances 1 Gm. daily is sufficient. The solution is supplied in a concentration of 4 Gm. of urethane in each 30 cc.

VITAMINS

Vitamin B_{12}

The search for the active principle of liver which is effective in the therapy of pernicious anemia has resulted in the isolation of a new nutritional factor. Recently it was discovered that *Lactobacillus lactis* Dorner required a certain factor (LLD) for growth, which factor was to be found in refined liver extracts in concentrations bearing an almost linear relationship to the unit potency of the extracts used in the treatment of pernicious anemia. The suggestion was made that this *"LLD factor"* might be the long sought active principle.

As a result of a long series of research studies a recent announcement was made which indicated the successful isolation from liver of a crystalline compound which, in microgram quantities, produces positive hematological response in initial tests in patients with

Addisonian pernicious anemia. This crystalline compound, named "vitamin B_{12}," has been found to possess high activity for the growth of *Lactobacillus lactis* Dorner. Consequently, that organism was selected for use as the medium for its testing. The factor was named *vitamin* B_{12} rather than "anti-pernicious anemia principle," because its biological role in the treatment of pernicious anemia or other disease is yet to be determined. Therefore vitamin B_{12} connotes only nutritional significance at present. In the future a name based upon chemical structure may be designated.

Vitamin B_{12} has been found to possess a potency of about 11,000,000 LLD units/mg. and 0.000013 mg./ml. of culture medium is capable of supporting half-maximal growth under the conditions used. As it crystallizes, the compound forms small red needles. The biological activity of this new vitamin is extremely high, in terms of its activity in clinical tests on pernicious anemia. One U. S. P. unit is defined as that amount of liver extract required daily to produce satisfactory clinical and hematological responses in Addisonian pernicious anemia. On the assumption that crystalline vitamin B_{12} is the only therapeutically active substance present an approximate equivalence of 1 μg. of the vitamin and 1 U. S. P. injectable unit can be expected. This relationship has been verified, as the clinical response obtained with single 3 and 6 μg. doses of vitamin B_{12} are not inconsistent with this equivalence. However, it must be kept in mind that 20 to 60 U. S. P. units of liver extract are given during the first 2 or 3 days to start remission of pernicious anemia in relapse which dosage is equivalent to not more than about 20 to 60 μg. of vitamin B_{12}.

Thiamine

Thiamine or vitamin B_1 has been available for a number of years and has been given in doses as high as 25 to 50 mg. with the thought that it would provide extra energy. A recent study has shown, however, that oral doses of more than 5 mg. daily are largely wasted. In addition continuous administration may result in an allergic response to the vitamin. Thiamine does play a leading role in metabolism and is one of the normal and essential constituents of animal and human tissue but it is very poorly absorbed in the gastro-intestinal tract so that 5 mg. daily is the maximum level of intake. This is just slightly less than 2 mg. per meal. The thiamine con-

tained in the food is included in this amount. This phenomenon is explained by the fact that the body either has developed no specific mechanism for absorbing this vitamin or has developed mechanisms barring the entry of harmful substances which also act as barriers to thiamine. This discovery will probably influence greatly the dosage schedules of thiamine.

Thiamine Dioctylsulfosuccinate

Vitamin B_1 has been produced in an oil-soluble form as thiamine dioctylsulfosuccinate according to a patent held by Merck and Co. This compound has approximately 60 per cent the vitamin B_1 activity of thiamine hydrochloride. It is soluble to a moderate degree in cottonseed oil, peanut oil, olive oil and cod liver oil, and highly soluble in alcohol, ether, acetone, choloroform, benzene, petroleum ether, ethyl oleate and other organic solvents. It has possible application in the preparation of concentrates with these solvents.

Riboflavin

Ever since the isolation of riboflavin as a separate entity the problem of solubility has been encountered since its comparative insolubility has prohibited the use of large doses in serious deficiency cases. New highly soluble forms of this vitamin were recently described thus allowing for much larger doses by parenteral routes. These new compounds are 100 to 1000 times as soluble as riboflavin itself so that 5 times the average requirements each day can be dissolved in 1 cc. of water. The riboflavin content of 100 quarts of milk (one of the richest natural sources) is matched by two teaspoonfuls of a solution of the new riboflavin.

Anti-ulcer Vitamin

The experimental inhibition of the development of peptic ulcers in guinea pigs has been attributed to an as yet unidentified vitamin U. Although it is not yet known whether the factor affects the human stomach in the same way, it is felt that the results warrant carefully controlled diet studies of human ulcer patients. The anti-ulcer factor is found in such foods as alfalfa, lettuce, kale, cabbage, other fresh

greens, fresh milk, raw egg yolk, wheat bran, soybean oil, olive oil, and liver fat. The factor is very readily inactivated by heat. In one experiment, a group of guinea pigs were given a diet made deficient in the vitamin by heating it. Another group received the same diet, unheated, with liberal supplements of food containing the factor. Results showed that 87.5 per cent of the group receiving the deficient diet had ulcer lesions. Only two of this group survived. None of the animals receiving the unheated, supplemented diet developed ulcer lesions. The question is raised as to whether or not the high incidence of peptic ulcers in human patients may be due, at least in part, to the fact that the major portion of food consumed is heat processed and only a very small amount of the food intake is raw.

Vitamin C

Ascorbic acid or vitamin C is another of those drugs for which new uses have been found. In doses of 100 mg. daily ascorbic acid has been found to prevent heat exhaustion entirely among 31 workers working under humidities of 50 to 84 per cent and temperatures of 100 to 105 degrees F. for a trial period of 29 days. A similar group of workers received sodium chloride in place of ascorbic acid but among this latter group of 42 workers there were 9 cases of heat exhaustion over the same period of time.

Animal Protein Factor

The search for effective drugs in the therapy of pernicious anemia has led to the discovery of an unidentified vitamin known simply as "Animal Protein Factor." It is related to the vitamin B family and is found in purified liver extract. Its production is brought about by the fermentation of certain immobile, rod-shaped bacteria. This vitamin was first discovered in hen houses where it was observed that in warm weather the hatchability of new chicks improved. This was traced to a bacterial fermentation taking place in the hen house litter. As research progressed it was shown that the vitamin was a constituent of liver extract. Control of the fermentation so that a bacterial extract could be developed for clinical trial was the next step. By using chickens as a guide a preparation for treating humans was finally produced and clinical tests are now being conducted. This new vitamin is under investigation by Lederle Laboratories. (Very recent work has shown this material to be identical with vitamin B_{12} discussed above.)

SEDATIVES—HYPNOTICS

Presidon

A new sedative hypnotic has recently been introduced which is not a barbiturate but a pyridine derivative having the chemical formula, 3,3-diethyl-2,4-dioxotetrahydropyridine. Marketed by Hoffmann-La Roche, Inc. as Presidon, this drug is a mild, quick-acting sedative-hypnotic which is reassuringly well tolerated. Because of its relatively short action and rapid elimination, there is very little likelihood of "hangover" or other side reactions. It is available in scored tablets of 0.2 Gm. each and is administered in doses of 0.2 to 0.4 Gm. shortly before retiring for insomnia; 0.1 to 0.2 Gm. for premature awakening or broken sleep or for daytime sedation.

ANTACIDS

Titralac

Antacid medication has been the target of many investigations. Recently there has been made available a new antacid which acts on the same principle as does milk (considered to be one of the most efficient gastric antacids) in the management of conditions characterized by gastric hyperacidity. This product, known as Titralac, contains glycine 30 per cent as a buffer and calcium carbonate 70 per cent as an alkalinizing factor and produces an acid-neutralizing curve closely simulating that of milk. In the presence of acid, glycine binds hydrogen ions, thus:

$$\text{Glycine} + H^+ + Cl^- \rightleftarrows \text{Glycine } H^+ + Cl^-$$

The pH of a pure solution of glycine is between 6 and 7. On addition of acid, the characteristic, smooth buffer curve of an ampholyte is obtained.

Calcium carbonate provides a potent reserve of acid-neutralizing power to supplement and maintain the buffering capacity of glycine. The result is a rapidly instituted antacid effect plus sustained action and relief is quick and prolonged. Titralac is administered in dosages of 1 or 2 tablets (each containing 0.15 Gm. glycine and 0.35 Gm. calcium carbonate) after meals or when symptoms appear. It is available from Schenley Laboratories, Inc.

RADIOACTIVE COMPOUNDS

The age-old adage, "It's an ill wind that blows nobody good," is only too true of atomic energy. Although the application of this energy in war is so disastrous it does have certain beneficial uses in many phases of endeavor and particularly in medicine. The beneficial effects have been divided into two main classes: the medical and biological advances and the provision of industrial power from nuclear fuels rather than from coal, oil or water. The compounds used are known as radioisotopes. An isotope is a variation of the chemical atom having a different atomic weight and physical proportions from the original element. The radioisotope or radioactive isotope not only has a different atomic weight but it also emits rays of a different type. A Geiger counter, an electroscope or an electrometer may be used to measure the quantity of isotopes present by counting or measuring the radiation emitted per unit time. Isotopes are prepared by bombarding the original atom with other atoms or they may result as waste products of the fission process in atomic piles. Radioisotopes are now being offered by the Isotopes Branch of the United States Atomic Energy Commission at Oak Ridge, Tenn., for research projects on their use in cancer.

There are several uses for radioisotopes in medicine such as tracing an element in the body; identification of a compound in which the traced element is combined; identification of stages in a series of biochemical processes; in diagnosis and in therapy.

The radioisotopes have shown great value in diagnosis. Radiosodium chloride designated as $Na^{24}Cl$ is injected intravascularly into the body in order to better study congestive heart failure, limitations of blood flow in ischemic areas and to measure the water content of the body. Compounds of radiostrontium, Sr^{89}, have shown possible value in diagnosing diseases of the bones and teeth and of tumors because they are deposited in the hard tissues of the body. Radiocarbon compounds, C^{14}, are employed similarly since they also are deposited in the bone as the carbonate. Sodium radioiodide, NaI^{131}, is of value in thyroid disease particularly in malignancy with metastases. The patient who is suffering from thyroid cancer is first x-rayed to determine where the cancer is located and to where it has spread. He is then instructed to go on a diet with low iodine content for a period of time. Following this small tracer doses of

radioactive iodine are administered and a Geiger counter used to determine whether the cancerous thyroid tissue will pick up the radioiodine. Some does and other does not. If it does pick it up then radioiodine therapy is indicated. Cretinism and mongoloid idiocy can be distinguished by means of this compound. In pathology there is being investigated the possibility of making direct photographic prints from thin sections of tissues in which radioactive compounds have been deposited. Radioiron, Fe^{59}, radiocobalt, Co^{55-58} and radiophosphorus, P^{32}, all show possible value in diagnosis.

Lysine is a common amino acid used as a building block for proteins. Recently it has been synthesized in a radioactive form at the University of Rochester. At present it is being used as a tracer with its course followed through the body because it is believed to have some role in cancer.

The radioactive elements also have been investigated for their therapeutic possibilities. Ordinary phosphorus or P^{31} enters particularly the tissues containing phospholipids. Radiophosphorus or P^{32} is also capable of this so that it is found in the red blood cells and in erythropoietic tissues. Here it is capable of selective irradiation to diseased tissue. For this reason P^{32} has been tested in blood dyscrasias such as leukemia and also in polycythemia vera. Persons suffering from a fatal type of leukemia have not been cured but they have been made to feel better. It has been shown that the average length of life after onset of the disease exceeds 4 years and many live 5 years or longer and a few 10 years. The radioactive phosphorus is given orally or intravenously. Although the irradiation delivered to abnormal tissues relative to that delivered to normal tissues is not so great as desired it does possess an advantage over x-ray in that the latter affects both tissues, resulting in radiation sickness. Weekly treatments have been shown to give the best results. As the disease is brought under control the intervals are prolonged.

Radiophosphorus also has been used externally by applying it to skin lesions such as carcinoma, hyperkeratosis, warts and hemangiomas. Over 90 per cent of the lesions disappeared. The chemical is applied by means of blotting paper of known dimensions soaked in measured amounts of radioactive sodium phosphate solution and dried.

Radioactive iodine or I^{131} has shown good results in the therapy of hyperthyroidism and possible value in thyroid adenoma with

metastases. Following diagnosis by means of tracer doses the radioiodine is given in therapeutic doses. It is administered in about three ounces of water which is carried to the patient in a glass in a lead container by means of long tongs. The glass is removed by means of the tongs, the patient takes the glass from the tongs and consumes the solution. The glass is rinsed 2 or 3 times and the patient also drinks the rinsings. Usually the radioiodine acts quickly reaching the thyroid tissues in 20 minutes or less. After it travels through the bloodstream the radioactive iodine is excreted, the urine being placed in lead containers for a period of time until the radioactivity decays. A report of a case of successful therapy of metastatic carcinoma of the thyroid with radioactive iodine given during a 3-year period revealed that the patient experienced disappearance of pain with increase in body weight and a progressive clinical change toward hypothyroidism following the last reported dose. Roentgenographic evidence pointed to an arrest if not a regression of the disease. No untoward effects followed the application of this therapy. The affinity of the thyroid cell for iodine was used as a basis for this "selective irradiation" therapy using a mixture of the isotopes I(130), half life 12.6 hours, and I(131), half life 8.0 days. Over the three-year period the patient received nearly 40,000 equivalent roentgens to each of his tumors. The basis for termination of radioactive iodine therapy was the lack of pick-up by any of the known metastases. Animal experiments are now under way to determine whether natural antibodies are capable of carrying radioiodine to special organs of the body such as the liver and kidney.

Radioactive gold, Au^{196}, Au^{198} and Au^{199}, has been tested in leukemia, lymphoma and Hodgkin's disease but no conclusions have been reached. Radiogold made up in a soft colloidal solution and injected by means of a needle into a malignant growth has been found to remain in the growth and to saturate the cancer without endangering the surrounding healthy tissues. The rays from this gold travel only a small fraction of an inch and kill all cancer cells which they hit. After a few days the rays die out. Some success in cancer therapy has been achieved in this fashion.

Radioactive antimony and arsenic are being investigated for their possible value in the therapy of tropical diseases, particularly filariasis. The former has been shown to kill off the parasites spawned within the infected organism and also to affect the sexual

organisms of the adult worms so that they cannot reproduce. Further clinical trials are being carried out and investigations in the therapy of other conditions such as schistosomiasis japonica are underway.

Radioactive materials are also employed in biological and medical research in the following ways: tagging experiments in studying the activity of viruses and bacteria, behavior of carcinogenic and antibiotic substances, stability of compounds, course of hydrogen atoms during oxidations and reductions and of carbon atoms during decompositions and linkages, localization of poisons in the body, absorption of medicaments and localization of atomic species normally in the body particularly in different cell parts; and in determination of how much of a stable isotope is present in the body. The radioactive substances are also of value in the study of radiation effects such as burns and radiation sickness with a view to the development of effective therapy.

Another possible application of radioactive materials is in increasing the effectiveness of medicinals given hypodermically according to recent reports.

ANTIHISTAMINICS

In the review immediately preceding this current summary the following antihistaminics were described briefly: Benadryl, Parke, Davis and Co.; Pyribenzamine and Antistine, Ciba Pharmaceutical Products, Inc.; Neoantergan, Merck and Co.; Hetramine, Pyridium Corp.; Hydryllin, G. D. Searle and Co.; Thephorin, Hoffmann-La Roche, Inc.; Thenylene, Abbott Laboratories; Histadyl, Eli Lilly and Co.; W53, William R. Warner and Co.; Chlorophen (Tagathen) and Bromophen, Lederle Laboratories. At that time Benadryl and Pyribenzamine were the only ones available on the market, the others being available for clinical trial only. During the year's period all have been marketed with the exception of Hetramine and Bromophen. W53 is now known as Diatrin; Wyeth Inc. have made available a modification of Hetramine known as Neohetramine, which chemically is (N,N-dimethyl-N′-p-methoxybenzyl-N′-2-pyrimidyl) ethylenediamine hydrochloride. Two new antihistaminics have also been made available namely: Decapryn which chemically is dimethylaminoethoxy-methyl benzyl-pyridine and is available from The William S. Merrell Co.; and Trimeton which chemically is phenyl-(2-

pyridyl)-(β-N,N-dimethylaminoethyl)-methane and is available from Schering Corp.

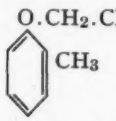
Many of these antihistaminics are also being marketed in the form of elixirs (indicated particularly for children) and in the form of creams and ointments for use in various skin disorders occurring as a result of an allergic reaction. Some tablet forms are coated to prolong their action. Nasal and ophthalmic solutions and expectorants of some are also available. Pyribenzamine when applied to the skin by iontophoresis has been found of value in pruritic dermatitis. Itching is diminished in intensity and the lesions are healed in most cases.

Encouraging results have been achieved with the use of antihistaminics in the palliation of allergic conditions but their use does not cure and therefore immunization still is necessary. Recent announcement was made by Dr. N. R. Ingraham, University of Pennsylvania Medical School, of the development of new ether-soluble extract injections which give a moderate and often effective degree of immunity from skin inflammations and allergies. The developments give hope for continuing relief to those who are allergic to certain plants and flowers that flourish during the waning months of the summer and early fall. Ether-soluble extracts of the plants and other substances are being used with success in treating contact dermatitis resulting from exposure to the offending substances.

MISCELLANY

Myanesin

Chemically known as α-β-dihydroxy-γ-(2 methyl-phenoxy)-propane, Myanesin has a structure as follows:



When first developed this drug was found to be of use in relaxing the muscles during anesthesia. There is a great deal of controversy over this product for this use and at present it is advised that it be used only by expert anesthetists. However further investigation has revealed a new approach to the therapy of neuro-muscular incapacity at any age. Given in therapeutic doses by oral administration

Myanesin has produced no significant side effects and does not influence the blood pressure, heart rate or respiration. Its administration has resulted in improvement in a number of patients with spastic conditions. Remarkable results have been achieved in the therapy of spastic and hyperkinetic disorders and in spastic, athetoid and choreiform types of cerebral diplegia. The drug does not remove the causes of the disorders but definite improvement is noted. The severity and level of the condition influences the period of effectiveness of this drug. Many patients will probably have to take it for the remainder of their lives. Originally introduced in England by British Drug Houses, Ltd., Myanesin is now under investigation by E. R. Squibb and Sons, Inc.

Terjolate

Individuals with very sensitive skins or those suffering from a dermatologic disorder frequently cannot use ordinary soaps for bathing or for household purposes. There have been available for some years various detergents for bathing purposes but no particular detergent for household purposes except for those usually found in the grocery stores. There has been marketed recently a detergent for cleansing dishes, greasy pots and pans, floors, laundry and other household cleansing for use by the individuals described above. This detergent known as Terjolate consists of sodium sulfate, sodium octodecanoate and N-diethanol-N-alkylamide and is a soapless, sudsing liquid. It is supplied in concentrated form so that one teaspoonful per gallon of water is usually sufficient. Rare Chemicals, Inc. are marketing Terjolate as a non-irritating and hypoallergenic detergent for household cleansing. It is sold through recognized drug trade channels.

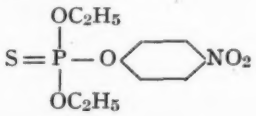
Gelatin Surgical Glove Powder

For many years surgeons have been seeking the ideal surgical glove powder. Many have been used but have always had some disadvantages. A recent study has suggested the possibility that the requirements for such a powder may be met by gelatin treated to render it insoluble but digestible under proteolytic action. Minimum water solubility and tackiness were observed when the gelatin powder was applied to damp hands. The gelatin was prepared by heating in an electrically controlled oven at 145° C. for more than 25 hours. When injected into the peritoneal cavities of rats all

traces of the powder were gone and no adhesions or granuloma had occurred 4 to 5 weeks later.

Thiophos

The use of DDT developed rapidly during the World War II and now it is widely employed for various purposes. Another compound, which is said to be 5 to 25 times more potent than DDT, is Thiophos 3422 also known as Parathion and E605. Chemically Thiophos is O,O,-diethyl O-p-nitrophenylthiophosphate for which the chemical formula is:



Thiophos is a high-boiling, deep brown to yellow liquid, some samples of which possess a characteristic odor. It is slightly soluble in water and completely miscible in many organic solvents such as acetone, ethyl ether, cyclohexanone, alcohols, esters and animal and vegetable oils; very slightly soluble or insoluble in petroleum ether, kerosene and refined spray oils. Thiophos is not readily destroyed by oxidation and it is quite stable to hydrolysis under normal conditions. It can be used in the form of a dust or as a spray when formulated into wettable powders. Thiophos has been given the generic title Parathion by the Council on Pharmacy and Chemistry of the A. M. A. and it is available from American Cyanamid Co.

Aluminum Salts of Bile Acids

Aluminum salts of bile acids have been investigated by White Laboratories because they have shown superior properties to those derived from other metals such as strontium, iron, silver and sodium. The aluminum bile acid salt is almost insoluble in the dilute acid of the stomach and is well tolerated when given orally. It is soluble in dilute alkalis and decomposes in the intestinal tract to form a water-soluble bile salt which promotes complete and rapid absorption of fatty material and also possesses other therapeutic value. As a result of the reaction aluminum hydroxide is also formed in the intestine which counteracts the cathartic action and diarrhea frequently brought about by other metal salts of bile acids and also permits

effective amounts of the aluminum bile acid salt to be administered safely.

Westsal

In various heart conditions it is necessary for the patient to limit himself to a restricted sodium or salt-free diet which after a time becomes very unpalatable and flat because of the lack of seasoning. Various salt substitutes have been introduced over a period of years. The latest of these substitutes to be developed is a liquid containing lithium chloride, citric acid and potassium iodide. It is claimed that it tastes exactly like salt. It may be sprinkled on the food at time of eating or it may be used in cooking and baking without the salt flavor being destroyed and without any impairment to the food. This new salt substitute is being marketed as Westsal by Westwood Pharmacal Corp.

Gravidox

One of the problems in pregnancy is the prevention of morning sickness or hyperemesis gravidarum. A product for this purpose was recently made available by Lederle Laboratories. Known as Gravidox it is available in tablet and ampul form. Each tablet contains 20 mg. each of pyridoxine hydrochloride and thiamine hydrochloride and the ampul contains in each cc. 50 mg. of each of the drugs.

Diaparene

Use of a new drug to eliminate the cause of diaper rash was announced in the last year. Diaper rash is regarded as the most common skin condition encountered in infants and young children. Its cause is said to be due to ammonia production from bacterial decomposition of the child's wetting. The strong ammonia odor as well as the skin irritation are commonly noted in the morning after the child has lain in a wet diaper for some hours. According to a recent report, a child may remain in a wet diaper, treated with this new drug, for as long as 15 hours without danger of diaper rash. Known as Diaparene the new product has as its active ingredient para-di-isobutyl cresoxy ethoxy ethyl dimethyl benzyl ammonium chloride monohydrate. It is marketed by Homemakers' Products Corp.

KNL, Darrow's Solution

Severe diarrhea in infants and young children results in a serious loss of body fluid associated with a marked loss of potassium in the urine. For this reason a new therapeutic product was developed to relieve this condition. KNL, Darrow's Solution contains in each 100 cc., 0.26 Gm. of potassium chloride, 0.4 Gm. of sodium chloride and 0.59 Gm. of anhydrous sodium lactate. It is sterilized and pyrogen-free so that it is suitable for intravenous administration. Its use has shown that it does not apparently shorten the period of watery diarrhea, but it does enable the babies to withstand a severe or prolonged attack that would otherwise be fatal. In a group of 50 infants treated with this solution only 3 died whereas in the control group of 53 treated by the usual methods there were 17 fatalities. It is necessary to give the solution slowly and only when the patient is well hydrated or symptoms of potassium intoxication may result. Since a potassium deficiency is noted in diabetic coma, indications are that KNL, which replaces lost potassium, would be useful in treating this condition. KNL, Darrow's Solution is available from Cutter Laboratories, Inc.

Gossypol

Gossypol is a compound separated from the pigment glands of cottonseed. It has been found in animals to inhibit the appetite and thus considerably reduce the food intake. When freshly prepared this compound has a low toxicity. Its action in inhibiting the appetite appears to be specific for no effect on the heart, lungs, kidneys or other parts of the body could be demonstrated. The possible use of this drug in the treatment of obesity has been suggested. This drug is another one of those unusual discoveries in that it has been an objectionable constituent of cottonseed meal which caused toxic symptoms when the meal was fed to cattle. Consequently the Southern Regional Research Laboratories were given the task of finding a method of removing it from the nutritious meal.

Botanein P

The Botany Mills Inc. recently announced the development of a potentially important new protein product, Botanein P, which contains 17 amino acids of which 9 are indispensable to body growth. Botanein P has a cystine content of almost 12 per cent, higher than

any other protein with the exception of insulin. It is the cystine which is believed to aid the renewal of skin surfaces. It is believed that this substance will prove of value pharmaceutically as an oral medicament to accelerate the growth of epithelial tissue (hair, skin, etc.) in case of burns or injuries to the skin due to exposure to the elements of nature (sun, wind, etc.). Botanein P is a yellow to light-tan amorphous solid, with little odor and no taste, insoluble in water but soluble in dilute alkalis and readily digested by enzymes such as trypsin, a proteolytic enzyme present in the pancreatic fluid.

Among human and general food uses indicated are: in cosmetics, especially suntan creams; as a food ingredient to accelerate and improve the growth of fur, feathers, etc. on animals; as a super-nutrient for cattle; as a medium for the growth of micro-organisms, e. g. yeast; as a research chemical, particularly in clinical research (e. g. diabetes, arteriosclerosis, etc.) as a starting material in the preparation of amino acids or protein hydrolysate mixtures; and as an adsorbing agent to be used in the clarification and purification of beverages. In the field of general usage, Botanein P is indicated as an agent to prevent corrosion; as a fixing agent for insoluble dyestuffs, lacquers, and pigments in calico or indigo printing; as an emulsifying agent to stabilize the dispersion of one liquid in another when these two liquids are immiscible; as a protective colloid which would act as a buffering agent thus stabilizing the pH of the solution while facilitating dispersion; and as an adhesive when put into solution.

BOOK REVIEWS

Organic Chemistry. By Hugh C. Muldoon, Sc. D.; Third Edition, 648 pages; 1948. The Blakiston Co., Philadelphia and Toronto. Price, $5.50.

Textbooks of organic chemistry suitable for use by students in schools of pharmacy, medicine or dentistry are rare. Some present a formal course in organic chemistry with few references to medicinals. Others give only medicinals with insufficient underlying theory. This latest edition of Dr. Muldoon's text is a skillful combination of both organic chemistry and the chemistry of organic medicinals so that it would seem to be an ideal text for students in the medical sciences.

The text is arranged in the accepted sequence for the study of organic chemistry such as is found in most modern texts. The various medicinals are integrated into their proper position and discussed along with other related chemicals. This helps the student fit the substances into their chemical classification and to better understand their properties. The text has been brought into agreement with the U. S. P. XIII and the N. F. VIII. Many non-official but important drugs are also included.

The chapters devoted to proteins, vitamins, steroids, antibiotics, etc. give evidence that the book has been carefully re-written and modernized. Spot checks on some of the most recent medicinals showed all of them to be present.

The author is to be complimented on the excellence of this text, its clarity of style and format and its high standard of accuracy. Teachers of organic chemistry in professional schools would do well to examine it for possible adoption. Practitioners will find it a valuable reference for their libraries.

L. F. Tice

Textbook of Pharmacognosy. By Heber W. Youngken A. M., Ph. M., Ph. D., Sc. D.; Sixth Edition, 1063 pages; 1948. The Blakiston Co., Philadelphia and Toronto. Price, $8.50.

One, in the United States, can scarcely think of pharmacognosy without thinking of both the many original investigations carried out

by H. W. Youngken and his text, long the standard in the field of pharmacy. This the sixth edition (first edition, 1921) is a revised version of the fifth. The publisher's note explaining certain type changes on pages which were not entirely reset is commendable but the average reader is likely to overlook it entirely.

The text is arranged in the same order as previous editions but Dr. Youngken has revised the text in a very complete fashion deleting the more obsolete monographs and adding new ones and new technics. New subjects added are Allergens and Allergenic Preparations, Antibiotics and Bacterial Biological Products, and Pollen grains, their structure, staining and mounting. The entire text is in agreement with the U. S. P. XIII and the N. F. VIII.

The book is probably misnamed for it is far too encyclopedic to be considered as simply a textbook. This does not imply that it cannot be used as a text for the teacher may use only those parts which are essential. The use of the book as an authoritative reference would seem as important as its use as a text and many will value it for this purpose. So well known is this standard work that the reviewer needs to do little else than announce the new edition. Its high quality is equally well known and the sixth edition is no exception to the established reputation which it enjoys.

L. F. Tice

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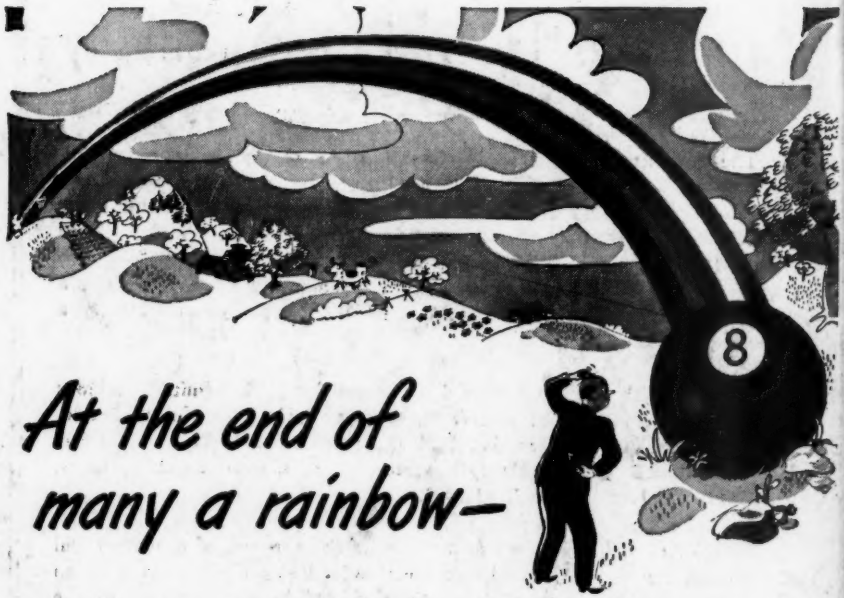
100 "	4.25	7.00	14.00	15.00	100 " 6.50
250 "	5.25	9.00	18.75	20.00	250 " 10.25



At the end of many a rainbow—

IF YOU GO to the end of a rainbow, so the fairy tales say, you'll find a pot of gold.

Of course, no grownup believes this. But it's surprising how many people believe what amounts to the same thing.

That is, many of us have a dreamy notion that somewhere, sometime, we'll come upon a good deal of money. We go along from day to day, believing that *somehow* our financial future will take care of itself.

Unfortunately, this sort of rainbow-chasing is much more apt to make you wind up behind the eight ball than with a pot of gold.

When you come right down to it, the only sure-fire way the average man can plan his financial security is through saving—and saving regularly.

One of the soundest, most convenient ways to save is by buying U. S. Savings Bonds through the Payroll Plan.

These bonds are the safest in the world. They mount up fast. And in just 10 years, they pay you $4 back for every $3 you put in!

P. S. You can buy U. S. Savings Bonds at any bank or post office, too.

SAVE THE EASY WAY... BUY YOUR BONDS THROUGH PAYROLL SAVINGS

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